

COOH terminus of human sIL-6R with the NH₂ terminus of human IL-6.--

[Please replace the paragraph beginning at page 6, line 27, with the following:]

--Fig. 2 shows the amino acid (SEQ ID NO:3) sequence (and DNA sequence (SEQ ID NO:4)) of a fusion polypeptide H-IL-6 according to the invention. Sequences for the restriction enzyme Sall (GTCGAC), the signal peptide (MLAVGCALLAALLAAPGAA) and the linker (RGGGGSGGGGSVE) are indicated. The linker links the COOH terminus of human sIL-6R with the NH₂ terminus of IL-6.--

[Please replace the paragraph beginning at page 6, line 35, with the following:]

--Fig. 3 shows the amino acid sequence of the IL-6 polypeptide (SEQ ID NO:5) present in a fusion polypeptide H-IL-6 according to the invention.--

Please replace the paragraph beginning at page 7, line 19, with the following:

--The DNA of fig. 1 was prepared. For this purpose, human IL-6R cDNA (Schooltink et al., Biochem. J. (1991) 277, 659-664) was used. This cDNA was cloned into the expression plasmid pCDM8 via restriction site Xho I (Müllberg et al., Eur. J. Immunol. (1993) 23, 473-480). By means of a polymerase chain reaction (PCR), an sIL-6R fragment was generated by using the primer (1) (pCDM8 5' primer: 5' TAATACGACTCACTATAGGG 3' (SEQ ID NO:6)) and primer (2) (sIL-6R 3' primer: 5'

CCGCTCGAGCTGGAGGACTCCTGGA 3' (SEQ ID NO:7)) under normal conditions.

After being cut with restriction enzymes Hind III and Xho I, this fragment was cloned into the open plasmid pCDM8. The plasmid pCDM8-sIL-6R formed. Thereafter, a second PCR reaction was carried out with IL-6 cDNA which has also been cloned into the expression plasmid pCDM8 by using Xho I. The primers (3) (IL-6-5' primer: 5' CGGCTCGAGCCAGTACCCCCAGGAGAA3' (SEQ ID NO:8)) and primer (4) (pCDM8 3' primer: 5' CCACAGAAGTAAGGTTCTT3' (SEQ ID NO:9)) were used. The PCR product was cut with restriction enzymes Xho I and Not I and cloned into plasmid pCDM8-sIL-6R. The plasmid pCDM8-sIL-6R-IL-6 formed. Thereafter, a synthetic linker was prepared which consisted of two oligonucleotides: primer (5) (5' TCGAGGAGGTGGAGGTTCTGGAGGTGGAGGTTCTGGAGGTGGAGGTTCTG 3' (SEQ ID NO:10)) and primer (6) (5' TCGACAGAACCTCCACCTCCAGAACCTCCACCTCCAGAACCTCCACCTCC3' (SEQ ID NO:11)). Oligonucleotides (5) and (6) were combined according to standard methods into a double strand and then cloned into the plasmid pCDM8-sIL-R-IL-6 digested by the restriction enzyme Xho I. The plasmid pCDM8-H-IL-6 formed.

Please replace the paragraph beginning on page 8, line 4, with the following:

The DNA of fig. 2 was prepared. For this purpose, the steps as described in Example 1 were carried out. However, the following primers were used instead of primers (5) and (6), respectively: primer (7) (5' TCGAGGAGGTGGAGGTTCTGGAGGTGGAGGTTCTG 3' (SEQ ID NO:12)) and primer (8) (5'